MASTER'S DEGREE THESIS

Master of Science in Advanced Mathematics and Mathematical Engineerinhe

Title: A Mathematical Model of the Spread of Two Viral Sub-types on a Plant Leaf *(Numerical Simulation)*

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A Mathematical Model of the Spread of Two Viral Sub-types on a Plant Leaf

Numerical Simulation

Master Thesis

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Abstract

Key words: Mathematical Biology, Epidemiology, Virus Dynamics

Whilst in humans free virus particles and host cells are assumed to be homogenously mixed, in plants, the spatial component is a key factor. The natural proliferation of the virus through a plant is known to happen from a cell to an adjoining cell. When several strains of a virus are present on a plant leaf, the co-infection of a cell by two sub-types is extremely rare. The mechanism which prevents this co-infection is not known in detail. A mathematical model is constructed by modifying the typical Fisher-Kolmogorov equation to understand this mechanism. Two equations are considered, one for each strain. They include the supression of the competitor's type by modifying the reproduction terms in the Fisher-Kolmogorov equations. The hypothesis of co-infection of cells by two viral strains on a plant leaf being extremely rare is tested for the mathematical model presented in this paper. Running simulations of the model shows that this hypothesis is only verified in the symmetric case of the considered rectangular 2-dimensional domain. This means that this model only verifies the hypothesis for the case where both strains are taken at corners of the rectangular domain and when both strains assume equal coefficients. For any biologically realistic case, this mathematical model does not show positive results and is not able to verify the hypothesis.

Contents

1

Introduction

The importance of mathematical modelling is becoming more recognised with time as it is applied to solve many situations in an increasing amount of fields. A good model may give us useful information on how the system of interest works in depth. Consequently, this might allow us to make sense of data, verify experimental hypothesis and make predictions among many others. In particular, models in epidemiology allow us to understand how viruses spread within and between hosts. Mathematical models in epidemics have helped decision makers in predicting the outcome of different vaccination programmes and in preventing problems that might appear in the future [1].

Viruses infect hosts which can be as diverse as bacteria, fungi, plants, insects and humans. In the particular case of plants, viruses can infect their host in many different ways. Nevertheless, the natural proliferation of the virus through a plant occurs from some small sector of infected cells to the neighbouring cells and tissues [5]. The virus is then passed from an infected to a healthy host, which can happen in many different ways. During the winter, for example, viruses typically propagate through seeds or pollen of infected plants [4]. However, most plant viruses are transmitted by insects or fungal pests [11]. The main reason for which we study plant viruses is to understand how they cause many important plant diseases which have had a big impact on crop production [4].

The **objective of this thesis** is to analyse the behaviour of two viral subtypes (a wild type and a mutant) on a plant leaf. For this we construct a mathematical model

which is suitable for this situation. The model consists of two coupled reaction-diffusion equations, one for each strain. A numerical simulation of the system in 2-dimensions is then carried out (a 2-dimensional model is considered since on a plant leaf the third dimension is negligible). Experimental results suggest that co-infection of a cell by two viral subtypes is extremely rare [2]. Since this is a biological plausible factor, this idea is included within the model. Both equations therefore include the suppression of the reproduction of its competing type.

Motivation of the thesis : The mechanism preventing the co-infection is not known in detail and this is what is studied in depth in this paper. The hypothesis suggesting that co-infection of a cell by two viral subtypes is unsual is tested. Considering the results of the study by J.C. Cantero and A.Korobeinikov [3], in which the previous hypothesis was confirmed in a 1-dimensional symmetric case, it seems relevant to test the same hypothesis but in the more realistic 2-dimensional case.

Organization

- Chapter 2 covers the biological background of viruses in general and viruses in plant leaves, which is required to understand the mathematical model presented in this project.

- Chapter 3 introduces the basic Fisher-Kolmogorov equations which are widely used in biological systems that describe spatial spread as occurs in this project.

- Chapter 4 introduces the main model of this project which is obtained by modifying the Fisher-Kolmogorov equations. The suppression of proliferation of a viral subtype by its competing type is considered for both strains at this stage.

- Chapter 5 deals with the linear stability analysis of the model introduced in Chapter 4. At this stage, the stability analysis neglects diffusion. This analysis helps understanding the results which are presented later in the paper.

- Chapter 6 introduces the numerical method used to solve the model presented in Chapter 4 and shows details of the numerical simulation. The main challenge of this project has been highly computational.

- Chapter 7 shows some of the results of the numerical simulation and they are discussed.

- Chapter 8 a more detailed stability analysis, including the diffusion terms, is presented.

- Chapter 9 some further results and discussion are shown and also a more biologically realistic result is presented.

- Chapter 10 provides the conclusion of this paper.

- Chapter 11 proposes an exploration of ideas to carry out further research in the same field.

- Chapter 12 offers an appendix including the fortran code used to compute the numerical simulation of the model presented in Chapter 4.

- Chapter 13 provides the references.

2

Biological Background

1. Viruses

Despite viruses being the cause of many serious illnesses in humans, they have also been a key factor in the research of molecular and cellular biology [11]. A virion is a complete infectious virus particle. It consists of a small piece of nucleic acid wrapped in a protein coat which is known as a capsid or nucleocapsid [4, 11]. The genetic information of the virus is held in the nucleic acid genome and can be of type DNA or RNA [4, 11]. Furthermore, the virion can also have another protective layer surrounding the protein coat called lipid envelope. An important remark about viruses is that they are not capable of self-reproduction but they rely on a host organism for proliferation [7]. A host is a living organism which is susceptible to getting infected with the virus.

2. Replication cycle of viruses

The steps for the virus to replicate itself depends on each virus; however, there are some general steps which most viruses undergo for its self-replication. To begin with, the viral proteins of the surface of the virus manage to stimulate the various enzymes in the susceptible cell attaching the virus to the target or host cell [7]. The virion is then injected into the cell and immediately afterwards, it is uncoated in order for the viral genome to be reachable. Once the genetic information of the viral genome is read by the nucleus of the

cell, the host cell starts producing viral proteins and copies of the viral genome [7]. These newly produced viral proteins are then used to provide the protein coats and envelopes of the new virus particles. Finally, when these new virus particles are successfully created, they leave the host cell looking for new target cells.

2.1 Mutation in viruses

Most of the times, the new virions created are not exact copies of the original virus. Mutations of viruses are frequent and they occur randomly rather than being an act of survival. The interaction of more than one sub-type of the virus is therefore typical in hosts. Each of these sub-types of the virus is known as a viral strain. In a plant, it is common to have the interaction of a wild strain and a mutant strain, two sub-types of the virus. As mutations in plant viruses are frequent, so are interactions between strains on a plant leaf. In plants, the interaction between two different viruses has different properties from the interaction between two viral strains of a virus [2]. The latter is the one considered in this paper.

3. Plant viruses

The proliferation of viruses is different for different hosts. Furthermore, the virus particle-host cell interaction is also quite particular for each host and each virus. In humans or animals, target cells and free virus particles are assumed to be homogeneously mixed. In contrast, plant viruses affect their hosts in a different way. The spatial component is a key factor in the spread of these viruses through their hosts. The natural proliferation of plant viruses starts from a small sector of infected cells and spreads to the neighbouring cells and tissues; infecting, eventually, the rest of the plant [5].

The first step of the life cycle of the plant virus is the entrance of the virion into the cell [4]. Plant virions are not capable of entering the cell wall by themselves, since no receptors in the plant cells have yet been identified [11]. In contrast to viruses affecting humans and animals, plant virions enter the cell with the aid of some external factors. Typically, insects cause structural damage to the cell, providing an entry route for the virus [4, 11]. Once the virus particle enters the cell, the replication cycle of viruses takes place.

In order for the plant virus to increase its chances of successfully proliferating through its host, it must infect as many host cells as possible [6]. Once a cell is infected and copies of the virus particle are generated, the next move of the virus is to infect nearby cells. The virions move from one cell to the neighbouring cells via the plasmodesmata (PD) which are the channels that connect cells [6, 10]. To finally infect parts of the plant which are further away, the plant must enter the vascular system and when it do so, then the plant virus has successfully infected its host [4, 6].

3

Basis Model Without Supression of Competitor's Strain

In this study, the Fisher-Kolmogorov equation serves as a basis model, since diffusion is used in many biological system models to describe spatial spread [9]. The Fisher-Kolmogorov equations were first created to describe the propagation of an advantageous gene in a population space in 1 dimension. In this particular case, the system is considered in 2-dimensions since the third dimension on a plant leaf is negligible. Two viral strains are considered: u, the wild strain, and v, the mutant strain, where each strain is described by a reaction-diffusion equation. The system is analysed in cartesian coordinates.

$$\frac{\partial u(x,y,t)}{\partial t} = \mu_1\Big(\frac{\partial^2 u(x,y,t)}{\partial x^2} + \frac{\partial^2 u(x,y,t)}{\partial y^2}\Big) + a_1 u(x,y,t)(1 - b_1 u(x,y,t))$$

$$\frac{\partial v(x,y,t)}{\partial t} = \mu_2\Big(\frac{\partial^2 v(x,y,t)}{\partial x^2} + \frac{\partial^2 v(x,y,t)}{\partial y^2}\Big) + a_2 v(x,y,t)(1 - b_2 v(x,y,t))$$

Where $u(x,y,t)$ and $v(x,y,t)$ are both virus concentrations for the wild and mutant sub-type respectively; μ_1 and μ_2 are the diffusion coefficients for strains u and v respectively; a_1 and a_2 are the per capita reproduction rate of their viral strain; $b_1 = \frac{1}{K_1}$ and $b_2 = \frac{1}{K_2}$ where K_1 and K_2 are the carrying capacities of $u(x,y,t)$ and $v(x,y,t)$ respectively, which means the maximum possible capacity of the corresponding population.

4

Model With Supression of Competitor's Strain

In a plant, a double or multiple infection of a cell by two different viral sub-types is known to be extremely unusual [2]. Biological experiments certify that there should be some mechanism preventing the co-infection of a cell. Therefore, the model should in some way integrate this factor. Strain v should not propagate in the areas for which strain u has already infected the plant, and vice versa.

The corresponding reproduction term for u is then

$$a_1 u(1 - q_1 v)(1 - b_1 u - v)$$

and for v is

$$a_2 v(1 - q_2 u)(1 - b_2 v - u)$$

So the system of equations that is considered consists of two coupled reaction-diffusion equations which have the following form, where $u = u(x, y, t)$ and $v = v(x, y, t)$

(1)
$$\boxed{\begin{aligned}\frac{\partial u}{\partial t} &= \mu_1\Big(\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2}\Big) + a_1 u(1 - q_1 v)(1 - b_1 u - v)\\ \frac{\partial v}{\partial t} &= \mu_2\Big(\frac{\partial^2 v}{\partial x^2} + \frac{\partial^2 v}{\partial y^2}\Big) + a_2 v(1 - q_2 u)(1 - b_2 v - u)\end{aligned}}$$

The system is considered on a rectangular domain of 2-dimensions with $x \in [0, 1]$ and $y \in [0, 1]$ and with no-flux boundary conditions around the whole domain since clearly there is no flux flowing outisde a plant leaf. The boundary conditions hence have the form

$$\frac{\partial u(0, y, t)}{\partial x} = \frac{\partial v(0, y, t)}{\partial x} = 0$$

$$\frac{\partial u(1, y, t)}{\partial x} = \frac{\partial v(1, y, t)}{\partial x} = 0$$

$$\frac{\partial u(x, 0, t)}{\partial y} = \frac{\partial v(x, 0, t)}{\partial y} = 0$$

$$\frac{\partial u(x, 1, t)}{\partial y} = \frac{\partial v(x, 1, t)}{\partial y} = 0$$

5

Linear Stability Analysis with Absense of Diffusion

For model (1) given in the previous chapter, where both strains depend on (x, y, t), the stability conditions are obtained. First of all, the stationary uniform solutions $(\bar{u}, \bar{v})$ must be found for the model. These stationary solutions are obtainted by setting all partial derivates to zero in equations (1), leading to the following equations where some functions f_1 and f_2 are introduced:

$$f_1(\bar{u}, \bar{v}) = a_1 \bar{u}(1 - q_1 \bar{v})(1 - b_1 \bar{u} - \bar{v}) = 0 \tag{2}$$
$$f_2(\bar{u}, \bar{v}) = a_2 \bar{v}(1 - q_2 \bar{u})(1 - b_2 \bar{v} - \bar{u}) = 0$$

For simplicity purposes, it is considered that $b_1 = b_2 = 1$. Then the following stationary uniform solutions can easily be deduced from the set of equations (2) given above.

$$(\bar{u}_1, \bar{v}_1) = (0, 1) \qquad (\bar{u}_2, \bar{v}_2) = (1, 0) \qquad (\bar{u}_3, \bar{v}_3) = (\frac{1}{2}, \frac{1}{2})$$

To obtain the closest linear system where (u, v) is close to $(\bar{u}, \bar{v})$, the arbitrary infinitesimal perturbations ϵ and η are introduced where:

$$\epsilon(x, y, t) = u(x, y, t) - \bar{u} \qquad \text{and} \qquad \eta(x, y, t) = v(x, y, t) - \bar{v} \tag{3}$$

The next step is to consider approximations of $f_1(u,v)$ and $f_2(u,v)$ near any stationary solutions $(\bar{u},\bar{v})$. Multivariable calculus may be used to obtain the following approximations:

$$f_1(u,v) \approx f_1(\bar{u},\bar{v}) + \frac{\partial f_1}{\partial u}\epsilon + \frac{\partial f_1}{\partial v}\eta$$

$$f_2(u,v) \approx f_2(\bar{u},\bar{v}) + \frac{\partial f_2}{\partial u}\epsilon + \frac{\partial f_2}{\partial v}\eta$$

Second order and higher terms may be neglected since infinitesimal perturbations are considered. Recalling equations (2), $f_1(\bar{u},\bar{v}) = f_2(\bar{u},\bar{v}) = 0$, the approximations of f_1 and f_2 are therefore given by:

$$f_1(u,v) \approx \frac{\partial f_1}{\partial u}\epsilon + \frac{\partial f_1}{\partial v}\eta \qquad \text{and} \qquad f_2(u,v) \approx \frac{\partial f_2}{\partial u}\epsilon + \frac{\partial f_2}{\partial v}\eta$$

Finally, substituting in the equations defining the perturbations (3) into the equations defining the main model (1), leads to the following set of equations showing how the perturbations will evolve in time:

$$\frac{\partial \epsilon}{\partial t} = \mu_1\left(\frac{\partial \epsilon^2}{\partial^2 x} + \frac{\partial \epsilon^2}{\partial^2 y}\right) + \frac{\partial f_1}{\partial u}\epsilon + \frac{\partial f_1}{\partial v}\eta \tag{4}$$

$$\frac{\partial \eta}{\partial t} = \mu_1\left(\frac{\partial \eta^2}{\partial^2 x} + \frac{\partial \eta^2}{\partial^2 y}\right) + \frac{\partial f_2}{\partial u}\epsilon + \frac{\partial f_2}{\partial v}\eta$$

In this section, the stability is analyzed in the absense of the diffusion term. In Chapter 8, the same model is analyzed including this term since after the results given in Chapter 7, it will be clear that a more detailed analysis is beneficial.

Therefore, for this section, the sign of the eigenvalues of the Jacobian matrix given by the following matrix A, will give the conditions on the stability of the stationary solutions.

$$A = \begin{bmatrix} \dfrac{\partial f_1}{\partial u} & \dfrac{\partial f_1}{\partial v} \\ \dfrac{\partial f_2}{\partial u} & \dfrac{\partial f_2}{\partial v} \end{bmatrix}$$

Using equations (2) from above which define functions f_1 and f_2, the Jacobian matrix A is explicitly given by:

$$A = \begin{bmatrix} \Big(-a_1(1-q_1v)u \Big) & \Big(-a_1u(1-q_1v) \Big) \\ \Big(-a_2v(1-q_2u) \Big) & \Big(-a_2(1-q_2u)v \Big) \end{bmatrix}$$

Following the research conducted by Juan Carlos Cantero and Andrei Korobeinikov [3], only the stability conditions of the homogenous point $(\bar{u}_3, \bar{v}_3) = (\frac{1}{2}, \frac{1}{2})$ will be shown in this chapter. In Chapter 8, the stability of the other two homogenous solutions is analysed.

The Jacobian matrix A for the homogenous solution $(\bar{u}, \bar{v}) = (\frac{1}{2}, \frac{1}{2})$ is then:

$$A = \begin{bmatrix} \Big(-\frac{a_1}{2}\Big(1-\frac{q_1}{2}\Big) \Big) & \Big(-\frac{a_1}{2}\Big(1-\frac{q_1}{2}\Big) \Big) \\ \Big(-\frac{a_2}{2}\Big(1-\frac{q_2}{2}\Big) \Big) & \Big(-\frac{a_2}{2}\Big(1-\frac{q_2}{2}\Big) \Big) \end{bmatrix}$$

The determinant of this matrix is zero and so the condition for the homogenous solution to be stable is that the Trace $A < 0$. Therefore, the stability conditions for the homogenous solution $(\bar{u}, \bar{v}) = (\frac{1}{2}, \frac{1}{2})$ are the following:

$$a_1q_1 + a_2q_2 < 2(a_1 + a_2) \qquad \text{stable}$$

$$a_1q_1 + a_2q_2 > 2(a_1 + a_2) \qquad \text{unstable}$$

6

Numerical Method

Due to the non-linearity in the reproduction terms of both equations described by (1), it is not possible to obtain an explicit solution for the model. Hence, a numerical method is used to solve the model. The method used is the explicit finite difference method.

Explicit Finite Difference Method

For this method, only the numerical method of strain u is discussed but exactly the same results apply for strain v. Considering a rectangular domain in the (x,y)-plane where,

$$0 < x < 1 \qquad 0 < y < 1$$

and assuming no flux boundary conditons around the whole domain, $u(x, y, t)$ can be obtained using this method for all values of t as long as initial values, $u(x, y, 0)$ are given on the whole domain [8]. The rectangular domain is labelled by a uniform rectangular grid of points, spaced with Δx in the x-direction and Δy in the y-direction, where

$$\Delta x = \frac{1}{n_x} \qquad \Delta y = \frac{1}{n_y}$$

The approximate solution at a time $t = n$ is given by the following equations:

$$U_{r,s}^n \approx u(x_r, y_s, t_n) \qquad r = 0, 1, \ldots, n_x \qquad s = 0, 1, \ldots, n_y$$

By calculating the derivative in time using the finite difference method, the value of the function at the next time step is obtainted, which is what is needed to provide an apporoximation.

$$\frac{\partial u}{\partial t} = \frac{u^{n+1} - u^n}{\Delta t} + \mathcal{O}(\Delta t^2)$$

where $\Delta t = t_{n+1} - t_n$

The laplacian using this method is given below [8]:

$$\begin{aligned}\Delta u &= \frac{\partial^2 u(x,y,t)}{\partial x^2} + \frac{\partial^2 u(x,y,t)}{\partial y^2} \\ &= \frac{u(x_{r+1}, y_s, t_n) - 2u(x_r, y_s, t_n) + u(x_{r-1}, y_s, t_n)}{(\Delta x)^2} \\ &\qquad + \frac{u(x_r, y_{s+1}, t_n) - 2u(x_r, y_s, t_n) + u(x_r, y_{s-1}, t_n)}{(\Delta y)^2} + \mathcal{O}(\Delta x^4) + \mathcal{O}(\Delta y^4)\end{aligned}$$

For the reaction diffusion equation concerning strain u, the following iterative method is considered:

$$\begin{aligned}U_{r,s}^{n+1} \approx U_{r,s}^n + \frac{\mu_1 \Delta t}{(\Delta x)^2}\left(U_{r+1,s}^n - 2U_{r,s}^n + U_{r-1,s}^n\right) + \frac{\mu_1 \Delta t}{(\Delta y)^2}\left(U_{r,s+1}^n - 2U_{r,s}^n + U_{r,s-1}^n\right) \\ + a_1 \Delta t U_{r,s}^n\left(1 - q_1 V_{r,s}^n\right)\left(1 - b_1 U_{r,s}^n - V_{r,s}^n\right)\end{aligned}$$

where the approximate solution for strain v at time $t = n$ is given by $V_{r,s}^n$.

This method gives the value of the unknown strain u at time $t = n + 1$ at all points of the grid in the rectangular domain considered, $U_{r,s}^{n+1}$.

As a summary, using this method, each value at the grid at time $t = n+1$ is obtained from 6 other known values at time $t = n$, namely

$$U_{r,s}^n, U_{r+1,s}^n, U_{r-1,s}^n, U_{r,s+1}^n, U_{r,s-1}^n, V_{r,s}^n$$

Hence, given initial values at all the nodes of the rectangular domain, $u(x, y, 0)$, the iterative method described above is used to approximate values of the strain u for any time. Exactly the same method is used for strain v as mentioned at the beginning of the section.

Numerical Simulation of the Model

There is a computational gap if the problem is considered with the explicit finite difference method described above. Here, the spatial derivatives taken for the nodes at the boundaries, for time $t = n$, would normally need values outside the domain to obtain approximations at time $t = n + 1$. At least one of the terms out of the six needed to obtain these approximations is not known at the boundaries of the considered domain. The approximate values at time $t = n + 1$ at the boundaries must somehow be obtained using values inside the domain.

For the system of equations (1) which defines the main model used for this project, no flux boundary conditions are considered, this is used to solve the computational gap mentioned above. Let's now consider the boundary of the domain at $x = 0$. Since we have no flux boundary conditons over all the domain, the same can be applied to the other boundary nodes. Using the explicit method, at $x = 0$:

$$\frac{\partial u(0, y_r, t_n)}{\partial y} = \frac{u(0, y_{r+1}, t_n) - u(0, y_r, t_n)}{\Delta y} = 0$$

But also with a simple change of variable,

$$\frac{\partial u(0, y_r, t_n)}{\partial y} = \frac{u(0, y_r, t_n) - u(0, y_{r-1}, t_n)}{\Delta y} = 0$$

And so the following can be deduced at the boundary $x = 0$

$$u(0, y_{r+1}, t_n) = u(y_{r-1}, t_n)$$

For approximations of the laplacian at these boundary nodes, the property showed above is used. Then, all apporoximations at time $t = n + 1$ can be calculated since they are given by values inside the domain at time $t = n$.

For the implementation of these properties in the numerical method for the model, see the Appendix in Chapter 12, where the Fortran code developed in order to numerically solve model (1) is offered. These simulations required a big computational effort and this was the main challenge of this project.

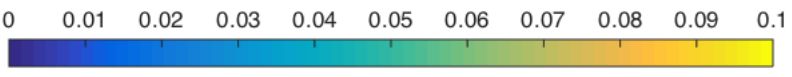
7

Results and Discussion

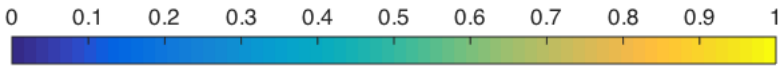
The natural proliferation of the strains occurs from a small sector of infected cells to the neighbouring cells. Moreover, it is observed that this proliferation occurs radially from the infected cells to the neighbouring target cells and tissues. Biologically, it would be logical to consider the case of the mutant strain v being somewhere close to the wild strain, since mutations occur randomly. But for this section, at first, the two viral strains are considered at the edges of the domain (the symmetric case). Juan Carlos Cantero and Andrei Korobeinikov [3] verified the hypothesis of the co-infection of cells being extremely rare in a 1-dimensional case. Their results motivated this project to be conducted in a more realistic 2-dimensional case. First, the numerical simulation will be carried out in order to show similar results and to verify the hypothesis for the symmetric case.

In all plots, the evolution of the spread of strain u will be shown on the left-hand side and of strain v in the right-hand side. Specific snapshots are shown for different times, which is considered to be dimensionless for the model.

Initially, both strains will be given a value of 0.1 in a small sector of the domain and this is shown in the plots with the yellow colour. In all initial snapshots for the plots for which $t = 0$, the following scale is used:

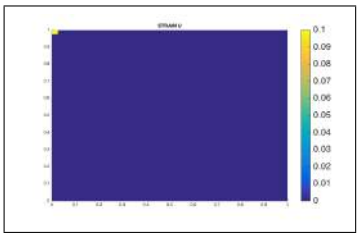
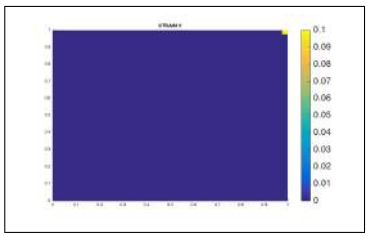


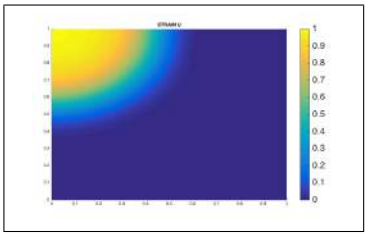
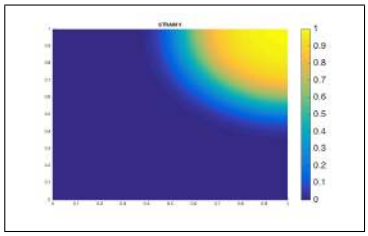
The rest of the plots have the following scale from 0 to 1 with the same colour range throughout the paper.

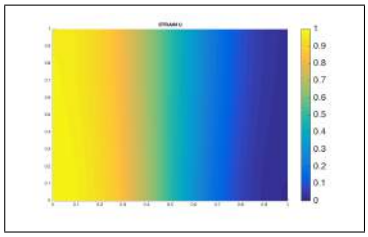
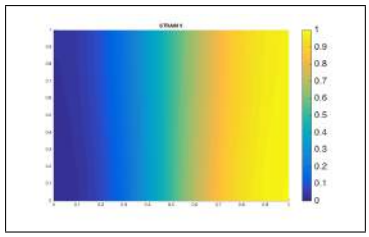


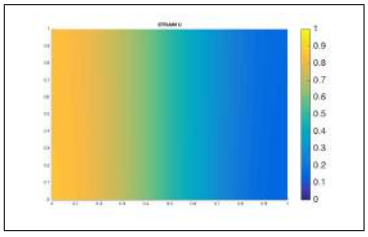
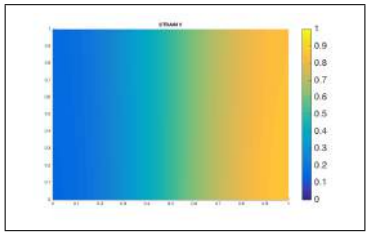
For the following two pages, the symmetric case is shown. Both set of snapshots, start of with each strain at one corner of the domain and at value 0.1. For the first set of snapshots, values of the coefficients leading to the stable case of the homogenous solution $(\bar{u}, \bar{v}) = (\frac{1}{2}, \frac{1}{2})$ is taken. It can be observed that after a large time, the system tends to this homogenous solution.

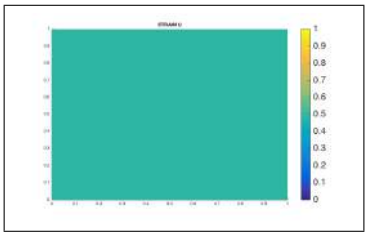
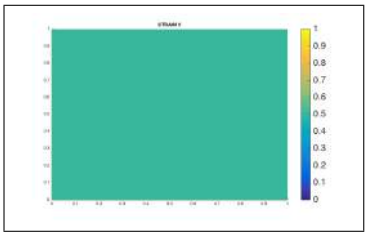
For the following snapshots, strain u is shown on the left, strain v on the right and the corresponding time is given on the same line. For the following plots, the following values of the coefficients are taken, $a_1 = a_2 = 1$, $q_1 = q_2 = 0.1$, $b_1 = b_2 = 1$, $\mu_1 = \mu_2 = 0.001$. These coefficients satisfy the stable condition of the homogenous solution $(\bar{u}, \bar{v}) = (\frac{1}{2}, \frac{1}{2})$ shown in Chapter 5.



$t = 0$

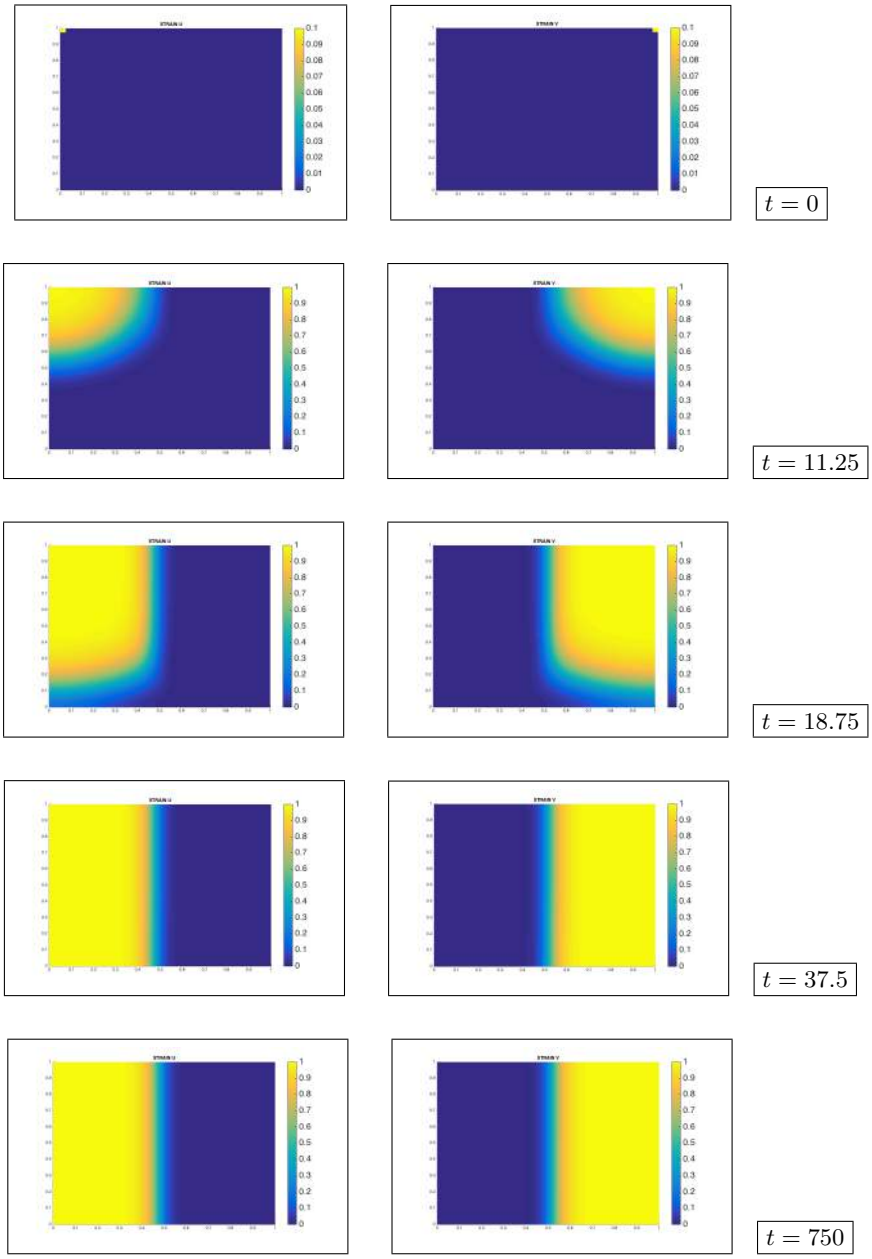


$t = 11.25$



$t = 37.5$



$t = 75$



$t = 750$

For the following 5 snapshots the symmetric case is still considered, so each strain is still taken at a corner of the rectangular domain. Furthermore, the coefficients take values, $a_1 = a_2 = 1$, $b_1 = b_2 = 1$ and $\mu_1 = \mu_2 = 0.001$. But compared to the previous snapshots, here larger values of q are taken, $q_1 = q_2 = 10$. These coefficients satisfy the unstable condition of the homogenous solution $(\bar{u}, \bar{v}) = (\frac{1}{2}, \frac{1}{2})$ shown in Chapter 5.



For the previous set of snapshots, there is a clear separation between both strains even after a very large time and the areas which are infected by strain u, are not infected by strain v and vice versa. In the first set of snapshots, where the coefficients take values to satisfy the stable case for the homogenous solution $(\bar{u}, \bar{v}) = (\frac{1}{2}, \frac{1}{2})$, after a large time, both strains infect the whole domain and there is multiple infection of cells as expected. Thus, depending on the values of the coefficients the unstable case of this homogenous solution seems to be achievable, which is the desired case for this project.

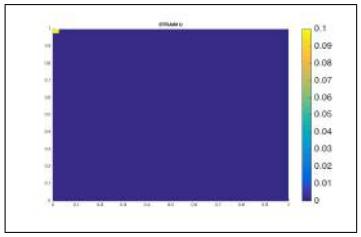
The last two sets of results were shown by Juan Carlos Cantero and Andrei Korobeinikov [3] in 1-dimension. This is what motivated this project to be carried out and the same results have been obtained in a more realistic 2-dimensional case. But, this is just the symmetric case where strains u and v are taken on each corner of the rectangular domain considered. This assumption is not biologically plausible. As mentioned in Chapter 3, mutations occur randomly and so it is more realistic to consider different coefficients for each viral sub-type as well as non-symmetric initial conditions.

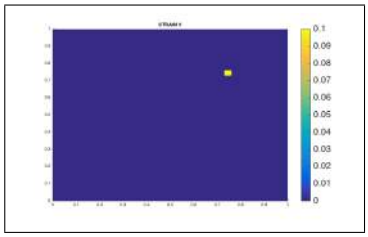
These results at first seemed to reassure the hypothesis of the co-infection of a cell by two viral sub-types being extremely rare. The system tending to either the stable or unstable case of the homogenous solution seemed to only depend on the value of the constants. However, the previous plots seem to work only for the symmetric case where both viral strains are taken at extreme corners of the domain and where the coefficients of both viral sub-types are the same.

Viral strain v was then moved at initial time and the system was consider in the non-symmetric case. The same constants as before are taken, where $a_1 = a_2 = b_1 = b_2 = 1$ and $\mu_1 = \mu_2 = 0.001$. In this chapter, results are shown for these values of coefficients and small values of q are taken, where $q_1 = q_2 = 0.1$. The analysis carried out in Chapter 5, suggests that the stable homogenous solution $(\bar{u}, \bar{v}) = (\frac{1}{2}, \frac{1}{2})$ should be approached for these coefficients. But, carrying out the simulation, it will be observed that different homogeneous solutions are acheived by just changing the inital conditions which shows that the hypothesis proposed in this project is not true.

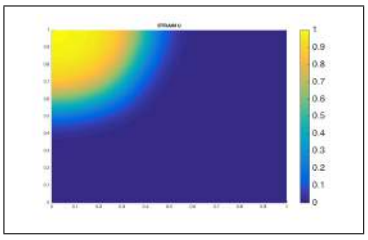
The two following sets of snapshots take different initial positions for strain v. It will be observed that the systems seem to tend to one of the other homogeneous solutions.

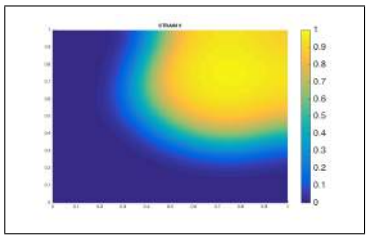
For the following two sets of snapshots, strain u will be still on the left-hand side and strain v on the right-hand side with the corresponding time of the snapshot in the right margin. For the following plots, the following values of the coefficients are taken, $a_1 = a_2 = 1$, $q_1 = q_2 = 0.1$, $b_1 = b_2 = 1$, $\mu_1 = \mu_2 = 0.001$.



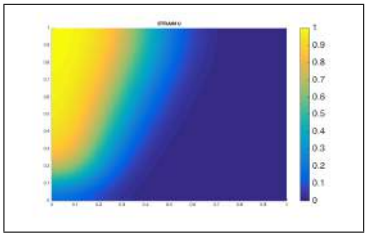


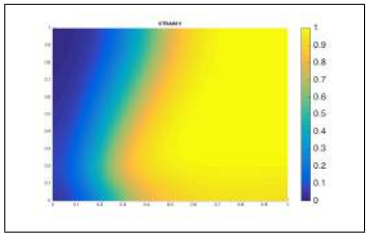
$t = 0$



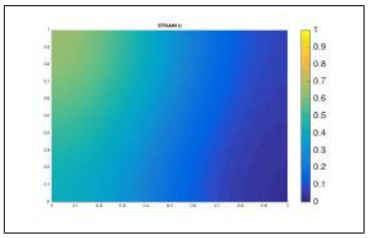


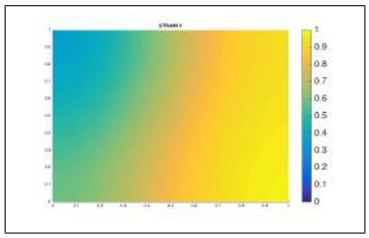
$t = 11.25$



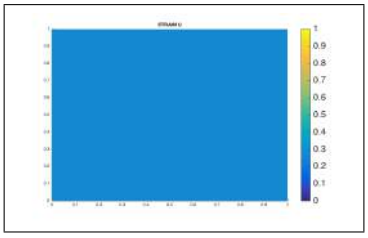


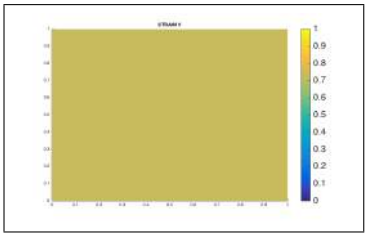
$t = 18.75$





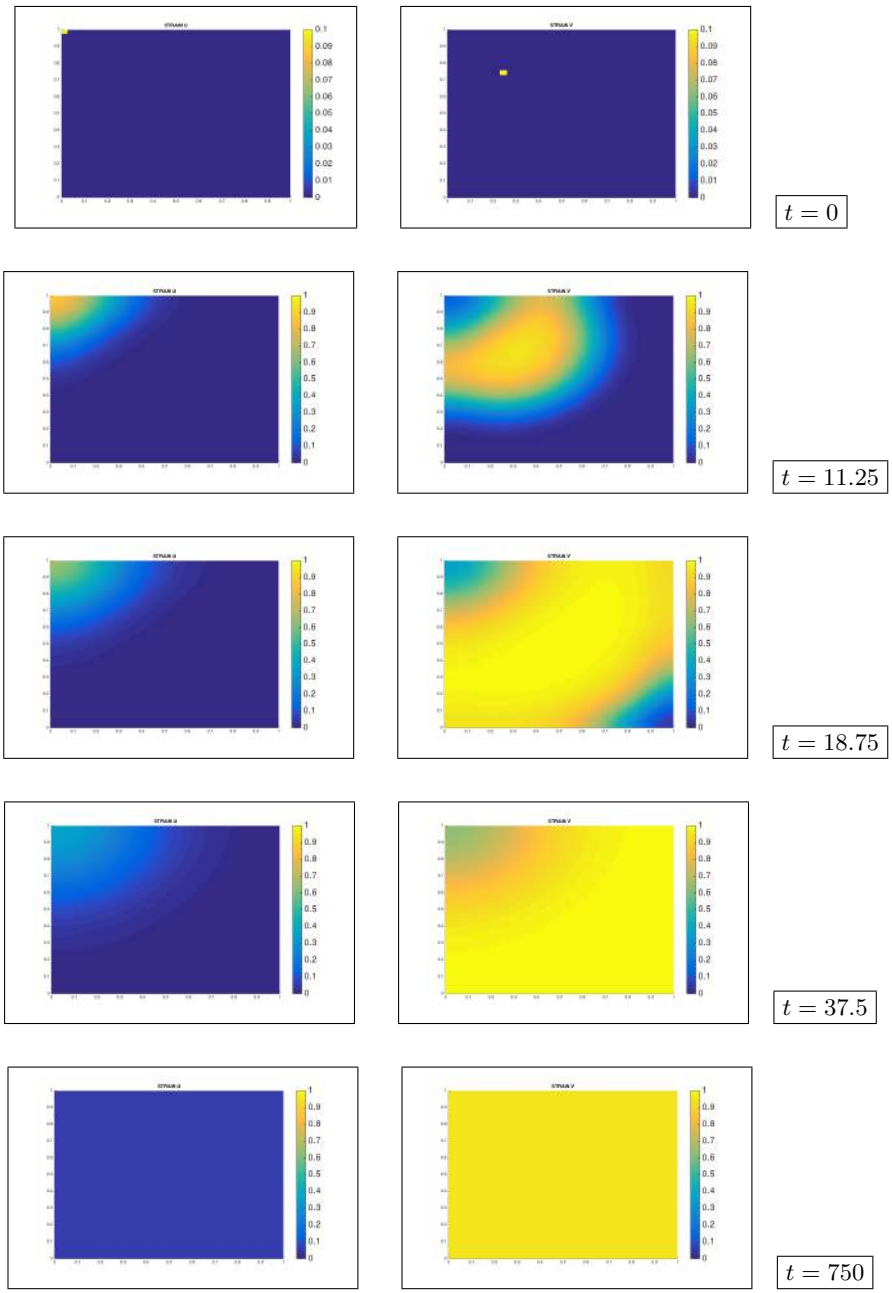
$t = 75$





$t = 750$

The following set of snapshots is very similar to the previous set with a slight difference in the initial condition for strain v. Both strains u and v still start off with initial values of 0.1. Strain u is still taken at a corner of the domain, but strain v this time starts off much closer to strain u. The same values of coefficients are taken, $a_1 = a_2 = 1$, $q_1 = q_2 = 0.1$, $b_1 = b_2 = 1$, $\mu_1 = \mu_2 = 0.001$.



In the last two sets of snapshots, there are differences in results by just varying the initial position of strain v. It can be observed that for values of coefficients suggesting stability of the homogeneous solution $(\bar{u}_3, \bar{v}_3) = (\frac{1}{2}, \frac{1}{2})$, after a large time the system tends to another solution. If the results of the simulation were as desired, there should be no differences in the behaviour of the system by just varying the initial conditions.

It can be observed that the closer strain v starts off from strain u, the more it tends to approach the homogeneous solution $(\bar{u}, \bar{v}) = (0, 1)$. This suggests that in the non-symmetric case this simulation does not outcome what is desired. For the considered coefficients, varying the initial position of the strains, causes the system to tend to the homogeneous solutions $(\bar{u}_1, \bar{v}_1) = (0, 1)$ or $(\bar{u}_2, \bar{v}_2) = (1, 0)$ depending on which strain has more area to spread in a given domain. The following chapter will show a more detailed stability analysis of the model by finding the stability conditions of the homogeneous solutions $(\bar{u}_1, \bar{v}_1) = (0, 1)$ and $(\bar{u}_2, \bar{v}_2) = (1, 0)$.

Once this detailed stability analysis is obtained, Chapter 8 will show a similar simulation to the previous two sets of snapshots. Large values of the coeffients q_1 and q_2 will be taken in order to satisfy the unstable case of the homogeneous solution $(\bar{u}_3, \bar{v}_3) = (\frac{1}{2}, \frac{1}{2})$.

8

Linear Stability Analysis Including Diffusion Coefficients

The perturbations introduced previously, equations (3), depend on time and the spatial coordinates. Furthermore, equations (4) show how these perturbations evolve in time. Since equations (4) have linear coefficients, the perturbations may be written as constants multiplied by an exponential in time and exponential in space of the following form:

$$\epsilon(x,y,t) = \epsilon_{\boldsymbol{\lambda}} e^{\sigma_{\boldsymbol{\lambda}} t} e^{i\boldsymbol{\lambda}(x+y)} \tag{5}$$

$$\eta(x,y,t) = \eta_{\boldsymbol{\lambda}} e^{\sigma_{\boldsymbol{\lambda}} t} e^{i\boldsymbol{\lambda}(x+y)}$$

The constants are $\epsilon_{\boldsymbol{\lambda}}$ and $\eta_{\boldsymbol{\lambda}}$ for perturbations ϵ and η respectively, $\sigma_{\boldsymbol{\lambda}}$ is the growth rate and $\boldsymbol{\lambda}$ is the wave number which is considered to be a 2-dimensional vector since 2-dimensional spatial coordinates are taken into account.

Substituting equations (5) into equations (4) from the previous chapter, which show how the perturbations evolve in time, the following is obtained:

$$\sigma_{\boldsymbol{\lambda}}\epsilon_{\boldsymbol{\lambda}} e^{\sigma_{\boldsymbol{\lambda}} t} e^{i\boldsymbol{\lambda}(x+y)} = \Big(\frac{\partial f_1}{\partial u} - 2\mu_1|\lambda|^2\Big)\epsilon_{\boldsymbol{\lambda}} e^{\sigma_{\boldsymbol{\lambda}} t} e^{i\boldsymbol{\lambda}(x+y)} + \frac{\partial f_1}{\partial v}\eta_{\boldsymbol{\lambda}} e^{\sigma_{\boldsymbol{\lambda}} t} e^{i\boldsymbol{\lambda}(x+y)}$$

$$\sigma_{\boldsymbol{\lambda}}\eta_{\boldsymbol{\lambda}} e^{\sigma_{\boldsymbol{\lambda}} t} e^{i\boldsymbol{\lambda}(x+y)} = \frac{\partial f_2}{\partial u}\epsilon_{\boldsymbol{\lambda}} e^{\sigma_{\boldsymbol{\lambda}} t} e^{i\boldsymbol{\lambda}(x+y)} + \Big(\frac{\partial f_2}{\partial v} - 2\mu_2|\lambda|^2\Big)\eta_{\boldsymbol{\lambda}} e^{\sigma_{\boldsymbol{\lambda}} t} e^{i\boldsymbol{\lambda}(x+y)}$$

Where the functions f_1 and f_2 are given in Chapter 5 in equations (2). Furthermore, the scalar product of the wave number with itself is given by $|\lambda|^2 = \boldsymbol{\lambda} \cdot \boldsymbol{\lambda}$ where by assumption this scalar quantity, $|\lambda|^2 \in \mathbb{R}$.

Dividing both equations by the exponentials in time and space, the following is obtained:

$$\sigma_{\boldsymbol{\lambda}} \epsilon_{\boldsymbol{\lambda}} = \Big(\frac{\partial f_1}{\partial u} - 2\mu_1 |\lambda|^2 \Big) \epsilon_{\boldsymbol{\lambda}} + \frac{\partial f_1}{\partial v} \eta_{\boldsymbol{\lambda}}$$

$$\sigma_{\boldsymbol{\lambda}} \eta_{\boldsymbol{\lambda}} = \frac{\partial f_2}{\partial u} \epsilon_{\boldsymbol{\lambda}} + \Big(\frac{\partial f_2}{\partial v} - 2\mu_2 |\lambda|^2 \Big) \eta_{\boldsymbol{\lambda}}$$

The following eigenvalue problem can then be considered:

$$\mathbf{A}_q \begin{pmatrix} \epsilon_\lambda \\ \eta_\lambda \end{pmatrix} = \sigma_\lambda \begin{pmatrix} \epsilon_\lambda \\ \eta_\lambda \end{pmatrix}$$

Where the Jacobian matrix $\mathbf{A}_q$ is now given by:

$$\mathbf{A}_q = \begin{bmatrix} \Big(\frac{\partial f_1}{\partial u} - 2\mu_1 |\lambda|^2 \Big) & \frac{\partial f_1}{\partial v} \\ \frac{\partial f_2}{\partial u} & \Big(\frac{\partial f_2}{\partial v} - 2\mu_2 |\lambda|^2 \Big) \end{bmatrix}$$

For simplicity purposes, it is still considered that $b_1 = b_2 = 1$, thus the following Jacobian matrix is obtained explicitly:

$$\mathbf{A}_q = \begin{bmatrix} \Big(-a_1(1 - q_1 v)u - 2\mu_1 |\lambda|^2 \Big) & \Big(-a_1 u(1 - q_1 v) \Big) \\ \Big(-a_2 v(1 - q_2 u) \Big) & \Big(-a_2(1 - q_2 u)v - 2\mu_2 |\lambda|^2 \Big) \end{bmatrix}$$

The determinant of this matrix is:

$$\mathrm{Det}\mathbf{A}_q = 4\mu_1 \mu_2 |\lambda|^4 + 2\Big(\mu_2 a_1 (1 - q_1 v)u + \mu_1 a_2 (1 - q_2 u) \Big) |\lambda|^2$$

In particular, the stability of the homogeneous solutions $(\bar{u}_1, \bar{v}_1) = (0, 1)$ and $(\bar{u}_2, \bar{v}_2) = (1, 0)$ is studied. The determinant of the matrix $\mathbf{A}_q$ given above is always positive for these

two homogeneous solutions given positive μ_1, μ_2, a_1 and a_2, which are assumptions for the main model (1).

Since for these particular homogeneous solutions $(\bar{u}_1, \bar{v}_1) = (0, 1)$ and $(\bar{u}_2, \bar{v}_2) = (1, 0)$ the determinant is always positive, the sign of the trace will determine their stability.

The trace for the homogeneous solution $(\bar{u}_1, \bar{v}_1) = (0, 1)$ is:

$$\text{Trace}\mathbf{A}_q = -a_2 - 2|\lambda|^2(\mu_1 + \mu_2)$$

and for $(\bar{u}_2, \bar{v}_2) = (1, 0)$ is:

$$\text{Trace}\mathbf{A}_q = -a_1 - 2|\lambda|^2(\mu_1 + \mu_2)$$

For both these homogeneous solutions, the trace is negative for all positive values of μ_1, μ_2, a_1 and a_2, which are assumptions of model (1). Therefore, both these homogeneous solutions are always stable. From the previous results in Chapter 6, it can be observed that by simply considering initially the non-symmetric case, the system tended to the homogeneous solution $(\bar{u}_1, \bar{v}_1) = (0, 1)$. This was due to the fact that this homogenous solution is always stable and will be always approached when considering any non-symmetric initial situation.

9

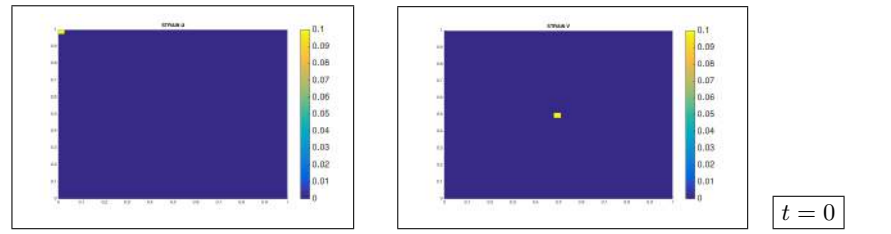
Further Results and Discussion

From the stability analysis shown in Chapter 6, it is now acceptable to say that the desired situation for this project is to take values of the coefficients satisfying the unstability of the homogeneous solution $(\bar{u}_3, \bar{v}_3) = (\frac{1}{2}, \frac{1}{2})$. This situation showed that the areas which were infected by strain u were not infected by strain v and vice versa after a long time.

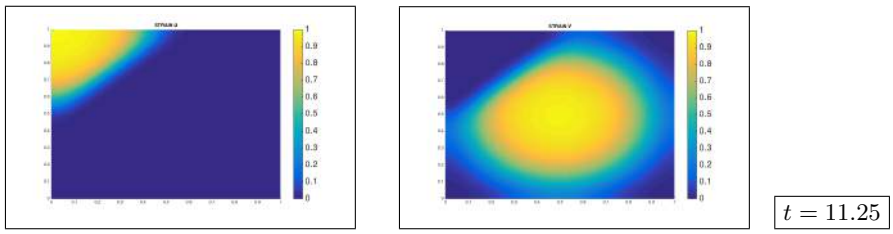
The situation mentioned previously, is only valid for the symmetric case. The following results will be taking the same values of coefficients in the non-symmetric case. This will show that one of the other two homogeneous solutions are approached considering the coefficients for the unstability of the homoegnous solution $(\bar{u}_3, \bar{v}_3) = (\frac{1}{2}, \frac{1}{2})$.

Biologically, it is plausible to take different coefficients for strains u and v. However, in this paper, results will just be shown for the non-symmetric initial position of the strains and equal coefficients for both strains. This will not show a separation of areas of infection for each strain since the homogenous solution $(\bar{u}_1, \bar{v}_1) = (0, 1)$ should be approached.

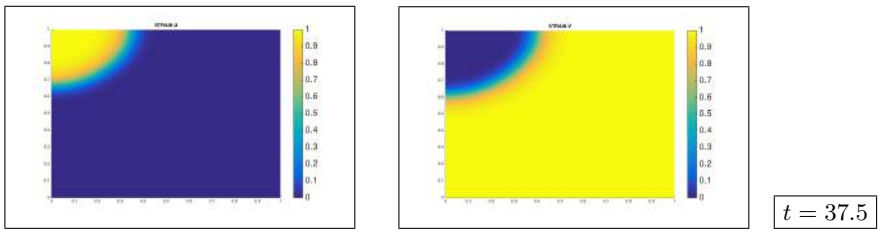
For the following snapshots, strain u is still on the left-hand side and strain v on the right-hand side. Here, the values of the coefficients are the following: $q_1 = q_2 = 10$, $a_1 = a_2 = 1$, $b_1 = b_2 = 1$ and $\mu_1 = \mu_2 = 0.001$. Initially strains u and v take values 0.1. Furthermore, strain u starts at a small sector in the top left corner of the domain and strain v in the middle of the domain.



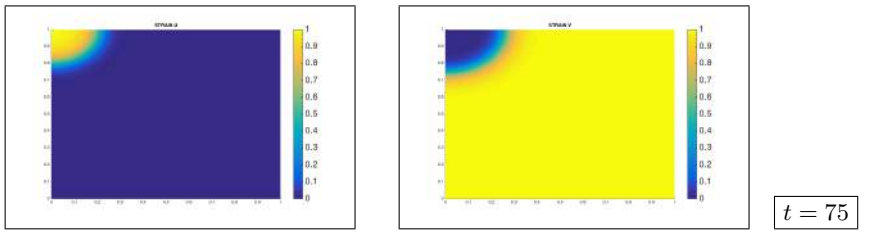
$t = 0$



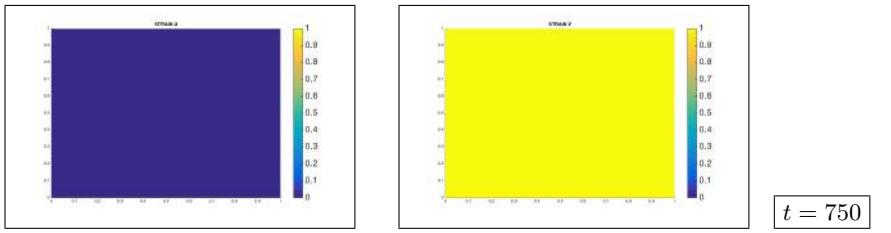
$t = 11.25$



$t = 37.5$

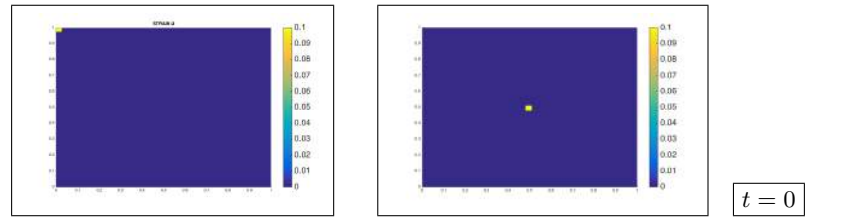


$t = 75$

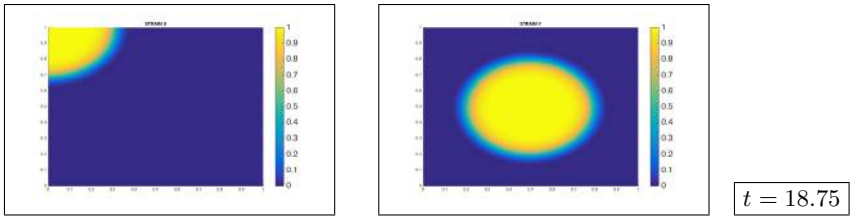


$t = 750$

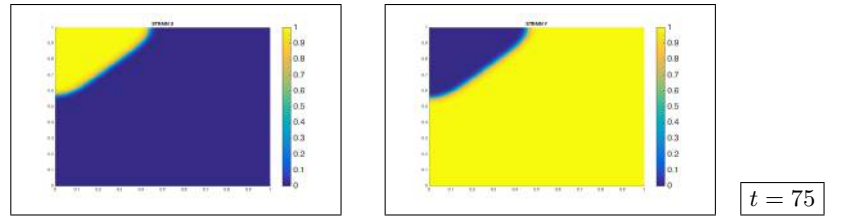
The previous set of snapshots allows to observe that for the values of the coefficients satisfying the unstable condition of the homogeneous solution $(\bar{u}_3, \bar{v}_3) = (\frac{1}{2}, \frac{1}{2})$ and non-symmetric initial conditions, the system tends to the homogeneous stable state $(\bar{u}_1, \bar{v}_1) = (0, 1)$. The next set of snapshots is the same simulation but taking smaller values for the diffusion coefficients, which is biologically more realistic. The values of the coefficients taken are the following: $q_1 = q_2 = 10$, $a_1 = a_2 = 1$, $b_1 = b_2 = 1$ and $\mu_1 = \mu_2 = 0.0001$.



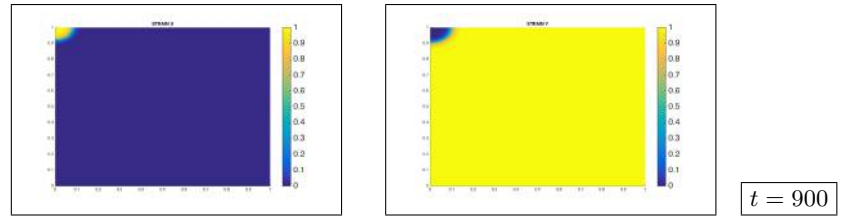
$t = 0$



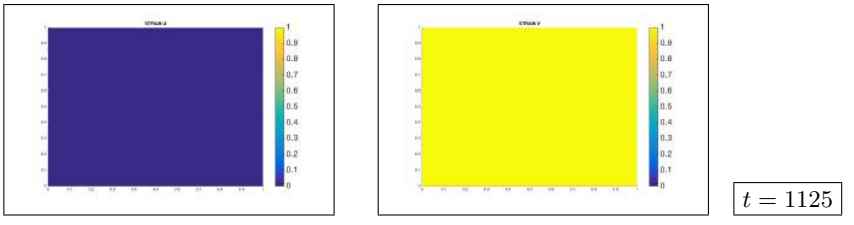
$t = 18.75$



$t = 75$



$t = 900$



$t = 1125$

It can be observed that fot the previous biologically more realistic case, the time taken to approach the homogeneous solution is much longer than in the first set of snapshots of this chapter where the diffusion coefficients were larger. Nevertheless, it can still be observed that eventually the system tends to the same homogeneous solution $(\bar{u}_1, \bar{v}_1) = (0, 1)$.

10

Conclusion

The aim of this thesis was to find a mathematical model verifying the hypothesis that co-infection of a cell by two viral sub-types is extremely rare. This has already been proved biologically [2] and this paper intends to find a correct model to understand the behaviour of this mechanism.

The project was motivated by a very similar project carried out by Juan Carlos Cantero and Andrei Korobeinikov [3]. In their case, they ran simulations of a very similar model to (1) but in one dimension. They obtained positive results to prove the hypothesis and this led to this project being carried out in a more realistic 2-dimensional case (the third dimension on a plant leaf is negligible).

After carrying out a stability analysis similar to the one they offered (neglecting the diffusion coefficients) stability conditions on the homogeneous solution $(\bar{u}, \bar{v}) = (\frac{1}{2}, \frac{1}{2})$ were obtained. Simulations of the model were then carried out on a rectangular 2-dimensional domain for the symmetric case. The symmetric case takes initial conditions for strains u and v in opposite extremes of the domain and same values of the coefficients for both strains. This led to similar results as achieved by Juan Carlos Cantero and Andrei Korobeinikov [3].

Then, the initial conditons were slightly changed and simulations were ran for this non-symmetric case. It was observed that the system tended to one of the other two homogeneous solutions. The project was concluded at this stage since the mathematical

model proposed in this project did not prove the desired hypothesis. The stability analysis proved that the homogeneous solutions $(\bar{u}_1, \bar{v}_1) = (0, 1)$ and $(\bar{u}_2, \bar{v}_2) = (1, 0)$ are always stable, no matter what values the coefficients take. This means that for any biologically realistic situation, the system would lead to one of these homogenous stable solutions and not give a separation of the proliferation of the two viral strains.

11

Exploration

A few suggestions on how this research could be improved are presented. The aim is to try to obtain positive results and be able to find a mathematical model which gives results that verify the hypothesis.

Using the Fisher-Kolmogorov equations for the mathematical model seems to be a good idea since diffusion is used in many biological system models to describe spatial spread. The Fisher-Kolmogorov equation has a travelling wave solution. A feature of this solution is that $u(x, y, t) \neq 0$ which holds everywhere except for at $u(+\infty, +\infty, t) = 0$. This property of the solution of a Fisher-Kolmogorov equation is not precise for the spread of a virus in a plant. One suggestion on how to make this solution more precise is to consider a density-dependent diffusion term of the form

$$\bigtriangledown \cdot (u^p \bigtriangledown u)$$

Where $p > 1$. The modified Fisher-Kolmogorov equation would then have the form:

$$\frac{\partial u}{\partial t} = \mu_1 \Big(\bigtriangledown \cdot (u^p \bigtriangledown u) \Big) + a_1 u(1 - b_1 u)$$

This, however, causes further computational difficulties.

Another suggestion is to change how the supression of the competitor's strain is introduced. In model (1), this supression is introduced in the reproduction term, but instead it could be introduced using impenetrable boundaries. This would be done by considering two moveable boundaries, one for each strain, which are taken to be impenetrable. This would prevent strain v from proliferating through areas already infected by strain u and vice versa. This approach would require two separate domains to be considered. For example, considering domain Ω_v, the values here of u could be considered to be less than 0.1. Similarly for the domain Ω_u where values of v are also considered to be less than 0.1. At each of these domains both Fisher-Kolmogorov equations would then have to be solved.

12

Appendix

This following code is the fortran code used in order to carry out the numerical simulation of this project. The code was run using Fortran90 and then the plots were produced using Matlab.

```
program main
  IMPLICIT NONE

  integer :: i,j,k
  integer ::nx=201,ny=201, nt=15000
  real :: dx=0.005, dy=0.005, mu1=0.0001, mu2= 0.0001, q1=10, q2
      =10, dt=0.0025
  real :: a1=1.0, b1=1.0, a2=1.0, b2=1.0
  real, dimension(:,:),allocatable :: x,y
  real, dimension(:,:,:), allocatable :: u,v
  real :: xc=0.0, yc=0.0
  allocate (x(nx,ny), y(nx,ny), u(nx,ny,nt), v(nx,ny,nt))
  open (2, file = 'smallmuuu.dat')
  open (10, file = 'smallmuuv.dat')
  open (12, file='smallmu.dat' )
```

```
!GENERATE A 2DMESH
  DO i=1,nx
     DO j=1,ny
        x(i,j)=xc
        y(i,j)=yc
        xc=xc+dx
     end do
     yc=yc+dy
     xc=0.0
  end do



  !Initial Conditions
  u=0.0
  v=0.0
 !u(nx,1,1)= 0.9
  !v(nx,ny,1) = 0.9
  u(nx 5:nx,1:5,1)=0.1
  v(97:102,97:102,1)=0.1
  !v(nx 5:nx,ny 5:ny,1)=0.1



  !
  ! for each new time step k, we use the previous time step k 1
  DO k=2,nt
     !COMPUTE INTERIOR NODES OF THE NEW U
     DO i=2,nx 1
        DO j=2,ny 1
           !U
```

```
        u(i,j,k) = u(i,j,k-1) + ((mu1*dt)/(dx ** 2))*(u(i+1,j
             ,k-1) - 2*u(i,j,k-1) + u(i-1,j,k-1)) + &
               ((mu1*dt)/(dy ** 2))*(u(i,j+1,k-1) - 2*u(i,j,k-1)
                    + u(i,j-1,k-1)) + &
               (a1*dt*u(i,j,k-1))*(1-u(i,j,k-1) - b1*v(i,j,k-1))
                   *(1-q1*v(i,j,k-1))
        !V
        v(i,j,k) = v(i,j,k-1) + ((mu2*dt)/(dx ** 2))*(v(i+1,j
             ,k-1) - 2*v(i,j,k-1) + v(i-1,j,k-1)) + &
               ((mu2*dt)/(dy ** 2))*(v(i,j+1,k-1) - 2*v(i,j,k-1)
                    + v(i,j-1,k-1)) + &
               (a2*dt*v(i,j,k-1))*(1-v(i,j,k-1) - b2*u(i,j,k-1))
                   *(1-q2*u(i,j,k-1))
    end do
end do
!
!COMPUTE LEFT BOUNDARY NODES OF THE U(N+1)
DO i=2,nx-1
    !U
    u(i,1,k) = u(i,1,k-1) + ((mu1*dt)/(dx ** 2))*(u(i+1,1,k-
         1) - 2*u(i,1,k-1) + u(i-1,1,k-1)) + &
          ((mu1*dt)/(dy ** 2))*(2*u(i,2,k-1) - 2*u(i,1,k-1)) +
               &
           (a1*dt*u(i,1,k-1))*(1-u(i,1,k-1) - b1*v(i,1,k-1))
               *(1-q1*v(i,1,k-1))
    !V
    v(i,1,k) = v(i,1,k-1) + ((mu2*dt)/(dx ** 2))*(v(i+1,1,k-
         1) - 2*v(i,1,k-1) + v(i-1,1,k-1)) + &
          ((mu2*dt)/(dy ** 2))*(2*v(i,2,k-1) - 2*v(i,1,k-1)) +
               &
          (a2*dt*v(i,1,k-1))*(1-v(i,1,k-1) - b2*u(i,1,k-1))*(1-
              q2*u(i,1,k-1))
end do
```

```
!

!COMPUTE RIGHT BOUNDARY NODES OF THE U(N+1)

DO i=2,nx 1
          !U
   u(i,ny,k) = u(i,ny,k 1) + ((mu1*dt)/(dx ** 2))*(u(i+1,ny
       ,k 1)  2*u(i,ny,k 1) + u(i 1,ny,k 1)) + &
        ((mu1*dt)/(dy ** 2))*(2*u(i,ny 1,k 1)  2*u(i,ny,k
            1)) + &
        (a1*dt*u(i,ny,k 1))*(1 u(i,ny,k 1)  b1*v(i,ny,k 1))
            *(1 q1*v(i,ny,k 1))
   !V
   v(i,ny,k) = v(i,ny,k 1) + ((mu2*dt)/(dx ** 2))*(v(i+1,ny
       ,k 1)  2*v(i,ny,k 1) + v(i 1,ny,k 1)) + &
        ((mu2*dt)/(dy ** 2))*(2*v(i,ny 1,k 1)  2*v(i,ny,k
            1)) + &
        (a2*dt*v(i,ny,k 1))*(1 v(i,ny,k 1)  b2*u(i,ny,k 1))
            *(1 q2*u(i,ny,k 1))
end do
!

!COMPUTE UPPER BOUNDARY NODES OF THE U(N+1)

DO j=2,nx 1
   !U
   u(1,j,k) = u(1,j,k 1) + ((mu1*dt)/(dx ** 2))*(2*u(2,j,k
       1)  2*u(1,j,k 1)) + &
        ((mu1*dt)/(dy ** 2))*(u(1,j+1,k 1)  2*u(1,j,k 1) +
            u(1,j 1,k 1)) + &
        (a1*dt*u(1,j,k 1))*(1 u(1,j,k 1)  b1*v(1,j,k 1))*(1
            q1*v(1,j,k 1))
```

```
    !V
    v(1,j,k) = v(1,j,k 1) + ((mu2*dt)/(dx ** 2))*(2*v(2,j,k
         1)  2*v(1,j,k 1)) + &
          ((mu2*dt)/(dy ** 2))*(v(1,j+1,k 1)  2*v(1,j,k 1) +
              v(1,j 1,k 1)) + &
          (a2*dt*v(1,j,k 1))*(1 v(1,j,k 1)  b2*u(1,j,k 1))*(1
              q2*u(1,j,k 1))

end do
!

! COMPUTE LOWER BOUNDARY NODES OF THE U(N+1)

DO j=2,nx 1
    !U
    u(nx,j,k) = u(nx,j,k 1) + ((mu1*dt)/(dx ** 2))*(2*u(nx
         1,j,k 1)  2*u(nx,j,k 1)) + &
          ((mu1*dt)/(dy ** 2))*(u(nx,j+1,k 1)  2*u(nx,j,k 1)
              + u(nx,j 1,k 1)) + &
          (a1*dt*u(nx,j,k 1))*(1 u(nx,j,k 1)  b1*v(nx,j,k 1))
              *(1 q1*v(nx,j,k 1))
    !V
    v(nx,j,k) = v(nx,j,k 1) + ((mu2*dt)/(dx ** 2))*(2*v(nx
         1,j,k 1)  2*v(nx,j,k 1)) + &
          ((mu2*dt)/(dy ** 2))*(v(nx,j+1,k 1)  2*v(nx,j,k 1)
              + v(nx,j 1,k 1)) + &
          (a2*dt*v(nx,j,k 1))*(1 v(nx,j,k 1)  b2*u(nx,j,k 1))
              *(1 q2*u(nx,j,k 1))
end do
!
!COMPUTING U(1,1) OF THE NEW TIME
!U
```

```
u(1,1,k)= u(1,1,k-1) + ((mu1*dt)/(dx ** 2))*(2*u(2,1,k-1)
     2*u(1,1,k-1)) + &
      ((mu1*dt)/(dy ** 2))*(2*u(1,2,k-1)  2*u(1,1,k-1)) + &
      (a1*dt*u(1,1,k-1))*(1-u(1,1,k-1) b1*v(1,1,k-1))*(1-q1*
          v(1,1,k-1))
!V
v(1,1,k)= v(1,1,k-1) + ((mu2*dt)/(dx ** 2))*(2*v(2,1,k-1)
     2*v(1,1,k-1)) + &
      ((mu2*dt)/(dy ** 2))*(2*v(1,2,k-1)  2*v(1,1,k-1)) + &
      (a2*dt*v(1,1,k-1))*(1-v(1,1,k-1) b2*u(1,1,k-1))*(1-q2*
          u(1,1,k-1))

!COMPUTE U(NX,1) OF THE NEW TIME
!U
u(nx,1,k)= u(nx,1,k-1) + ((mu1*dt)/(dx ** 2))*(2*u(nx-1,1,k
     -1)  2*u(nx,1,k-1)) + &
      ((mu1*dt)/(dy ** 2))*(2*u(nx,2,k-1)  2*u(nx,1,k-1)) +
          &
      (a1*dt*u(nx,1,k-1))*(1-u(nx,1,k-1) b1*v(nx,1,k-1))*(1-
          q1*v(nx,1,k-1))
!V
v(nx,1,k)= v(nx,1,k-1) + ((mu2*dt)/(dx ** 2))*(2*v(nx-1,1,k
     -1)  2*v(nx,1,k-1)) + &
      ((mu2*dt)/(dy ** 2))*(2*v(nx,2,k-1)  2*v(nx,1,k-1)) +
          &
      (a2*dt*v(nx,1,k-1))*(1-v(nx,1,k-1) b2*u(nx,1,k-1))*(1-
          q2*u(nx,1,k-1))

!COMPUTE U(1,NY) OF THE NEW TIME
!U
u(1,ny,k) = u(1,ny,k-1) + ((mu1*dt)/(dx ** 2))*(2*u(2,ny,k
     -1)  2*u(1,ny,k-1)) + &
```

```
      ((mu1*dt)/(dy ** 2))*(2*u(1,ny 1,k 1)  2*u(1,ny,k 1))
          + &
      (a1*dt*u(1,ny,k 1))*(1 u(1,ny,k 1)  b1*v(1,ny,k 1))*(1
          q1*v(1,ny,k 1))
!V
v(1,ny,k) = v(1,ny,k 1) + ((mu2*dt)/(dx ** 2))*(2*v(2,ny,k
     1)  2*v(1,ny,k 1)) + &
      ((mu2*dt)/(dy ** 2))*(2*v(1,ny 1,k 1)  2*v(1,ny,k 1))
          + &
      (a2*dt*v(1,ny,k 1))*(1 v(1,ny,k 1)  b2*u(1,ny,k 1))*(1
          q2*u(1,ny,k 1))

! COMPUTE U(NX,NY) OF THE NEW TIME
!U
u(nx,ny,k) = u(nx,ny,k 1) + ((mu1*dt)/(dx ** 2))*(2*u(nx 1,
    ny,k 1)  2*u(nx,ny,k 1)) + &
      ((mu1*dt)/(dy ** 2))*(2*u(nx,ny 1,k 1)  2*u(nx,ny,k 1)
          ) + &
      (a1*dt*u(nx,ny,k 1))*(1 u(nx,ny,k 1)  b1*v(nx,ny,k 1))
          *(1 q1*v(nx,ny,k 1))
!V
v(nx,ny,k) = v(nx,ny,k 1) + ((mu2*dt)/(dx ** 2))*(2*v(nx 1,
    ny,k 1)  2*v(nx,ny,k 1)) + &
      ((mu2*dt)/(dy ** 2))*(2*v(nx,ny 1,k 1)  2*v(nx,ny,k 1)
          ) + &
      (a2*dt*v(nx,ny,k 1))*(1 v(nx,ny,k 1)  b2*u(nx,ny,k 1))
          *(1 q2*u(nx,ny,k 1))



!
```

```
end do


!Write the desired snapshots into different files
!Matlab used to produce the plots of these matrices


write (2,*) u(:,:, 1)
write (2,*) u(:,:, 1500)
write (2,*) u(:,:, 3000)
write (2,*) u(:,:, 4500)
write (2,*) u(:,:, 6000)
write (2,*) u(:,:, 7500)
write (2,*) u(:,:, 9000)
write (2,*) u(:,:, 10500)
write (2,*) u(:,:, 12000)
write (2,*) u(:,:, 13500)
write (2,*) u(:,:, nt)
close(2)
write (10,*) v(:,:, 1)
write (10,*) v(:,:, 1500)
write (10,*) v(:,:, 3000)
write (10,*) v(:,:, 4500)
write (10,*) v(:,:, 6000)
write (10,*) v(:,:, 7500)
write (10,*) v(:,:, 9000)
write (10,*) v(:,:, 10500)
write (10,*) v(:,:, 12000)
write (10,*) v(:,:, 13500)
write (10,*) v(:,:, nt)
```

```
   close(10)

   write(12,*) u(:,:,nt)
   write(12,*) v(:,:,nt)
   close(12)



end program main
```

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